AMERICAN JOURNAL OF PHARMACY

PUBLISHED BY AUTHORITY OF THE

Philadelphia College of Pharmacy

HENRY KRAEMER, PH.D., Editor

VOL. 88 MAY, 1916 No. 5

CONTENTS.

Price, $3.00 per Annum, in advance. Issued in Monthly numbers of not less than 48 pages

SINGLE NUMBERS, 30 CENTS
BACK NUMBERS, 30 CENTS

Address all communications to
The American Journal of Pharmacy, 145 North Tenth Street, Philadelphia, Pa.

Entered at the Post Office at Philadelphia as second-class matter

American Journal of Pharmacy

ESTABLISHED IN 1825

Four preliminary numbers were published at different times until in 1829, when the publication of the regular volumes began. Since then the publication has been uninterrupted. During the period from 1829 to 1852 four numbers were published annually, except in 1847, when five numbers were published. From 1853 to 1870 six numbers were published. Since this time twelve numbers have been published annually.

Manuscripts should be sent to the Editor. It should be stated in this connection that the Editor does not assume any responsibility in connection with the views or investigations of contributors, other than to exercise general care in the selection of matter.

Contributors are allowed a reasonable number of copies of this JOURNAL, free of charge, if applied for when the proof is returned.

Reprints, if desired, must be applied for when the proof is returned. The table below shows the *approximate* cost of reprints, the make-up of the pages to be identically the same as in the JOURNAL. The actual cost may vary from the figures given, and will depend upon the amount of presswork, paper, binding, etc. Reprints containing half-tones may be expected to cost somewhat more than the rates given.

	2 pp.	4 pp.	8 pp.	16 pp.
25 copies . .	$2.25	$3.75	$7.75	$9.00
50 " . .	2.50	4.00	8.25	9.75
100 " . .	2.75	4.25	9.00	10.75
250 " . .	3.75	4.75	10.00	12.00

COVERS WITH TITLES	
25 copies . .	$1.75
50 " . .	2.00
100 " . .	2.25
250 " . .	2.75

THE AMERICAN
JOURNAL OF PHARMACY

MAY, 1916

THE POSSIBILITY AND VALUE OF IMPROVING THE COMMERCIAL BELLADONNA CROP THROUGH SELECTION.*

By ARTHUR F. SIEVERS, Chemical Biologist, Office of Drug-Plant Investigation, Bureau of Plant Industry, Washington, D. C.

The changes in trade relations of the United States which are expected to result from the European war will undoubtedly lead to the establishment here of industries the products of which have heretofore been imported from abroad. Among such industries may be mentioned the commercial growing of medicinal plants, and the impetus which war conditions have lent to such enterprises is already plainly felt. The sole source of many of our important drugs lies in that section of the world which is at present, and will be for some time to come, entirely unable to furnish the supply necessary for local consumption, and the result has been a steady rise in prices as the shortage has become more and more acute. Such prices have, as was to be expected, attracted attention to the possibility of domestic production of such products, and the efforts being made in that direction may lead to the establishment of permanent industries even after economic readjustments in Europe have resulted in more normal prices for such products.

The growing of drug plants differs greatly from the growing of the staple farm crops. In the first place, it requires an expert knowledge of a large number of plants, many of which are probably entirely unknown to the average agriculturist. The demand for any one plant is limited, and diversified farming would be necessary. Some of the plants can be grown only in limited areas in this country, and the methods of cultivation, harvesting, and preparation of the marketable

* Published by permission of the Secretary of Agriculture.

product require an expert knowledge of the habits and nature of the plants themselves and a thorough understanding of the proper methods to be employed to bring the crops into such condition as will make them acceptable to the trade. It will be seen, therefore, that such an undertaking has little in common with the growing of wheat, corn, or other common farm crops.

It is to be expected that the enterprise will be undertaken by four different groups of individuals: First, the back-yard enthusiast who expects to make large profits from his idle back-yard by growing a few medicinal herbs at his leisure and selling them at fancy prices; second, the farmer who plans to devote a small area of his farm to the same purpose incidental to his general farming; third, the individual or corporation that would make a special business of drug-plant cultivation with the aid of proper equipment and scientifically-trained men; and, fourth, the pharmaceutical manufacturers who would undertake the work for the purpose of producing the raw material required in their business and thus make themselves independent of the crude drug market.

This paper deals with the cultivation of belladonna, not from the agricultural standpoint, but from the standpoint of plant breeding and the improvement of the therapeutic quality of the drug produced by means of recognized methods of selection. Here again the problem involved differs greatly from the methods of selecting such crops as corn and other cereals. In the latter case the average farmer can select his seed readily by choosing the best ear of corn or head of wheat merely by physical characteristics. This, at least, will determine the yield per acre, which is the main factor in his profit. With a medicinal plant like belladonna, however, the quality of the product, from a therapeutic standpoint, cannot be determined by physical appearances, but requires chemical analyses. To make these analyses laboratory facilities and trained analysts are necessary. It is true, a physical selection may result in increased tonnage per acre, but the present tendency is to base the value of the crops on its alkaloid content. It is evident that methods of selection of alkaloid productiveness cannot be made by small growers included in groups one and two mentioned above, and the subject of this paper is therefore presented with a view to interesting the larger growers who have the facilities to make the analyses that are necessary.

It may not be amiss here to point out in what way the production of plants with a high alkaloid content is of great importance to the

grower. The great bulk of belladonna used in this country is bought as raw material for the manufacture of pills, plasters, tinctures, fluid-extracts, and for the manufacture of the pure alkaloids. It is of vital concern to the manufacturer of these products whether his raw material is high or low in alkaloids. While the Pharmacopœia guards against inactive material by requiring a minimum of 0.3 per cent. of alkaloids in the leaves, the large consumer is anxious to have the percentage as much above that as obtainable, because the greater the percentage of alkaloids in the raw material, the less material will be required to produce the finished product of the standard strength. The handling of less material will in turn result in a saving in the cost of manufacturing the products. It is evident, therefore, that the belladonna rich in alkaloids will command a better price.

The possibility of greatly adding to the value of crops of medicinal plants by increasing their active constituents by methods of selection led the Office of Drug-Plant Investigations of the United States Department of Agriculture to undertake a general study of this subject. While it was hoped that eventually something of benefit might be accomplished here, it was necessary to undertake a thorough experiment with a single plant as a start in order to demonstrate the feasibility of the plan. Belladonna was selected as a suitable plant for a number of reasons. It is an important plant and the supply from foreign sources is becoming more and more unsatisfactory, making domestic cultivation a necessity. It is readily cultivated and is thus well adapted to experimental purposes. It is a perennial, which fact makes it possible to study its constituents through a number of seasons, thereby getting a better basis for selection by eliminating to a great extent seasonal influences. Finally, its active constituents being alkaloids which can be definitely assayed by chemical means, a precise quantitative study of such constituents can be made.

The first step undertaken was to determine the range of variation in the percentage of alkaloids in individual plants; also the extent to which such variation is influenced by factors affecting the growth and cultivation of the plant. The quantitative study of the alkaloids was to be supplemented by a corresponding study of the physical or botanical characteristics of each individual in order to establish the relationship, if any, which exists between the physical and chemical characteristics of the plant.

In order to make the alkaloid determination for each plant some modification of the official method was necessary, owing to the smallness of the sample. In some cases only two grammes of dry material were available for the assay. In all cases the leaves were thoroughly air dried and then kept in a desiccator over sulphuric acid for 24 hours. The official method was modified as follows: The sample, from two to five grammes in weight, was placed in a 200-c.c. Squibbs separatory funnel, in which the maceration and percolation were done, thus avoiding the transfer of the material from a macerating flask to the percolator, thereby eliminating a serious source of error and saving a great deal of time.[1] For each gramme of material used 1 c.c. of dilute ammonia water was added.[2] The prescribed 50 c.c. of menstruum was added to start with, but the percolation was performed with three portions of 20 c.c. each to insure complete extraction.[3] The remainder of the process was in accordance with the Pharmacopœia.

In the summer of 1909 three rows of belladonna plants were started at Arlington, Va. They made a fair growth by fall, but failed to develop any seed. The following year they made a good growth, and 24 individual plants were staked out. They are designated as first-year plants, owing to their late start the preceding year. The only picking made from these plants in 1910 was in June, when they were in full bloom. When referring to this and subsequent pickings reference is made to leaves only.

Of the 24 plants, 1 assayed less than 0.400 per cent. alkaloids, namely, 0.334 per cent.; 7 less than 0.5 per cent., namely, 0.412, 0.440, 0.459, 0.462, 0.473, 0.485, 0.495 per cent.; 8 less than 0.6 per cent., namely, 0.503, 0.528, 0.536, 0.544, 0.555, 0.563, 0.587, 0.587 per cent., and 8 more than 0.6 per cent., as follows: 0.603, 0.618, 0.623, 0.645, 0.656, 0.657, 0.667, 0.700 per cent.

Results on Second and Third Years' Crops.

The first year's study having revealed a large variation in the alkaloidal content of individuals, a total of 59 plants was staked out in 1911, the original 24 and 35 additional in the same field. During this and the following season five pickings were made of all the individuals large enough. The first picking was made the second week

---

[1] A. F. Sievers, *Merck's Report*, Aug., 1910, p. 215.
[2] A. F. Sievers, *Journ. A. Ph. A.*, March, 1912, pp. 199–200.
[3] A. F. Sievers, *Ibid.*, March, 1912, pp. 199–200.

TABLE I.

Percentage of alkaloids in the leaves of individual belladonna plants at different stages of growth in 1911 and 1912.

Plant No.	Season of 1911						Season of 1912					
	Alkaloids (per cent.)						Alkaloids (per cent.)					
	First picking (May 12)	Second picking (May 22)	Third picking (June 17)	Fourth picking (Sept. 6)	Fifth picking (Oct. 17)	Average for season	First picking (May 10)	Second picking (May 21)	Third picking (June 18)	Fourth picking (Sept. 10)	Fifth picking (Oct. 17)	Average for season
1	.....	.....	.....	0.823	0.687	0.755	.....	0.332	0.503	0.653	0.417	0.501
2	0.852	0.698	0.583	.804	.619	.711	.....	.558	.700	.407	.606	.568
3	.384	.375	.277	.549	.451	.407	.....	.393	.448	.448	.....	.429
4	.461	.334	.304	.824	.665	.518	0.522	.557	.469	.654	.591	.559
5	.493	.700	.478	.681	.546	.579	.....	.438	.....	.510	.....	.474
6	.484	.....	.371	.630	.610	.524	.462	.415	.....	.548	.465	.472
7	.714	.622	.440	.765	.470	.602	.....	.424	.447	.689	.296	.464
8	.520	.618	.423	.891	.528	.596	.....	.....	.652	.726	.....	.689
9	.....	.627	.460	.781	.452	.580	.560	.384	.402	.501	.....	.429
10	.382	.344	.450	.671	.670	.503	.....	.421	.438	.457	.....	.420
11	.699	.677	.567	.537	.618	.619	.....	.388	.609	.692	.223	.499
12	.649	.782	.693	.497	.584	.641	.767	.631	.685	.715	.308	.638
13	.614	.627	.626	.763	.563	.639	.495	.479	.655	.472	.394	.518
14	.480	.556	.474	.476	.455	.488	.553	.421	.457	.359	.488	.420
15	.452	.....	.562	.546	.418	.494	.641	.531	.567	.462	.310	.550
16	.455	.754	.624	.622	.592	.609	.716	.631	.545	.....	.....	.631
17	.487	.....	.534	.396	.474	.473	.684	.591	.559	.....	.....	.611
18	.477	.645	.481	.634	.519	.551	.553	.386	.662	.....	.....	.534
19	.356	.386	.356	.507	.532	.427	.560	.423	.475	.....	.....	.486
20	.....	.489	.795	.509	.479	.568	.....	.676	.681	.....	.....	.678
21	.....	.535	.633	.669	.684	.630	.732	.719	.781	.....	.....	.744
22	.423	.410	.428	.454	.557	.454	.703	.593	.462	.....	.....	.586
23	.....	.348	.354	.487	.425	.403	.496	.366	.341	.....	.....	.401
24	.....	.349	.392	.....	.....	.370	.....	.....	.....	.....	.....	.....
25	.....	.277	.335	.....	.....	.306	.521	.438	.508	.....	.....	.489
26	.395	.378	.527	.797	.733	.567	.869	.700	.609	.....	.....	.726
27	.....	.287	.432	.554	.495	.442	.754	.693	.521	.....	.....	.656
28	.304	.392	.513	.740	.614	.513	.657	.535	.525	.....	.....	.572
29	.....	.655	.914	.908	.547	.756	.737	.647	.729	.....	.....	.704
30	.387	.573	.512	.653	.527	.530	.655	.553	.507	.....	.....	.572
31	.381	.430	.458	.669	.384	.464	.....	.....	.....	.....	.....	.....
32	.409	.425	.546	.703	.549	.526	.533	.446	.646	.....	.....	.542
33	.481	.447	.549	.496	.458	.486	.602	.589	.576	.....	.....	.589
34	.335	.....	.526	.532	.200	.414	.....	.292	.520	.....	.....	.406
35	.323	.476	.534	.768	.524	.430	.608	.596	.732	.590	.549	.616
36	.320	.468	.482	.488	.473	.446	.469	.418	.598	.555	.378	.483
37	.323	.423	.550	.719	.558	.515	.598	.442	.475	.705	.523	.548
38	.532	.514	.552	.749	.630	.595	.454	.463	.520	.586	.....	.506
39	.303	.262	.327	.614	.451	.391	.404	.365	.525	.600	.....	.473
40	.405	.395	.....	.797	.644	.560	.575	.556	.469	.....	.....	.533
41	.318	.390	.456	.562	414	.428	.508	.512	.524	.470	.332	.469
42	.494	.526	.497	.615	.528	.533	.617	.664	.648	.789	.....	.679
43	.515	.567	.534	.547	.331	.499	.506	.365	.698	.562	.....	.533
44	.342	.497	.448	.626	.550	.489	.458	.....	.467.	.....	.....	.463
45	.467	.410	.428	.759	.379	.488	.601	.501	.382	.430	.384	.460
46	.337	.285	.308	.588	.431	.390	.418	.334	.480	.483	.314	.406
47	.389	.422	.400	.573	.482	.453	.....	.479	.572	.449	.522	.505
48	.494	.493	.539	.748	.....	.568	.426	.346	.590	.567	.332	.452
49	.583	.476	.....	.668	.505	.558	.556	.476	.457	.578	.399	.481
50	.610	.583	.447	.619	.379	.527	.....	.361	.328	.420	.....	.353
1w	.638	.835	.587	.738	.612	682	737	.642	.777	.....	.....	.719
2w	.444	.769	.614	.311	.518	.531	.573	.544	.563	.....	.....	.560
5w	.464	.....	.741	.638	.595	.584	.741	.602	.524	.806	.647	.664
6w	.596	.879	.925	.711	.722	.766	.847	.747	.882	.804	.558	.768
7w	.558	.831	.832	.727	.571	.704	.782	.666	.646	.694	.573	.672
8w	.578	.717	.538	.570	.481	.577	.634	.453	.280	.505	.....	.468
9w	.487	.767	.553	.425	.337	.514	.557	.429	.638	.....	.....	.541
10w	.587	.763	.690	.473	.424	.587	.751	.478	.505	.639	.678	.610
11w	.425	.521	.373	.479	.420	.444	.773	.562	.430	.402	.....	.544
Average	.472	.528	.517	.633	.519	.532	.601	.503	.553	.568	.447	.545

in May, before many flowers had appeared. The second picking was made about two weeks later, when the plants were in full bloom, and the third picking during the third week in June, when the berries were well developed. At the time of the fourth picking, early in September, the plants had assumed their characteristic late summer appearance. The berries were ripe and the leaves were small and sparse. Later in the fall new leaves appear on the plants, and it was at this stage, during the third week in October, that the fifth and last picking was made. Table I gives the results of the analyses.

Relation of the Alkaloidal Content of the Leaves to the Stage of Growth of the Plant.

Opinions have been expressed from time to time as to the proper stage in the growth of the belladonna plant at which the leaves should be picked in order to insure the greatest percentage of alkaloids. Owing to the standard required by the Pharmacopœia, this is a question of no small economic importance. Gerrard[4] has found that the plant is not rich in alkaloids before flowering, but that the full development is reached at the period of flowering, and is maintained in both the roots and leaves into the fruiting season.

The large number of assays of the leaves of individual plants here involved presents exceptional opportunity for the study of the above question. The proper season for the picking of belladonna leaves does not, however, depend entirely on the percentage of active constituents present. This will become very evident when the data at

Table II.

Number of Belladonna Plants which Showed an Increase or Decrease in Percentage of Alkaloids in the Leaves at the Second, Third, Fourth, and Fifth Pickings as Compared with the Preceding Picking at Arlington Experimental Farm in 1911 and 1912.

Stage of growth	Season of 1911			Season of 1912		
	Total number of plants	Number of plants which showed—		Total number of plants	Number of plants which showed—	
		Increase	Decrease		Increase	Decrease
Second picking........	70	38	32	59	16	43
Third picking........	60	25	35	53	34	29
Fourth picking.......	54	40	14	32	20	12
Fifth picking.........	56	8	48	23	4	19

[4] Gerrard, A. W., "On the Alkaloidal Value of Belladonna Plants at Different Periods of Growth," *Yearbook of Pharmacy*, 1881–1882, pp. 400–404, 1882.

hand are thoroughly interpreted. Table II shows in condensed form the number of plants in which there was an increase or decrease in the percentage of alkaloids in the leaves at the various pickings.

Table II shows that in 1911 the leaves of most of the plants were richer in alkaloids at the second picking than at the first, which is in accord with the observations of Gerrard, already noted. In 1912, however, the opposite is true. It will be seen further that in the fourth picking of both years the greatest number of plants showed an increase in the alkaloidal content of their leaves. Referring to Table I, it is seen that in the fourth picking in 1911 the average quantity of alkaloids for the leaves of all the Arlington plants was 0.633 per cent., or more than one-tenth of 1 per cent. more than at the flowering stage. In 1912, at this same stage, the average was 0.568 per cent. of alkaloids, which is 0.065 per cent. higher than the average at the flowering stage. There appears to be but a slight difference, so far as the alkaloidal content is concerned, between the flowering stage and the early fruiting stage. At the last, or fifth, picking the plants had acquired much new growth and, judging from the average results, the percentage of alkaloids present in the leaves at that stage was not much different from the second and third stages.

Relation of Size and Appearance of Plants to Alkaloidal Content of Leaves.

When this investigation was first undertaken it was hoped that some relationship might be found to exist between the physical appearance of the plants and the alkaloidal content of their leaves, for, should such relationship exist, the process of distinguishing between the good and the poor plants with regard to their active constituents would become a much simpler matter than by use of the assay method, since the latter is necessarily tedious.

The variations in the physical appearance of belladonna plants depend largely on the height and the number of stalks or stems. When height is referred to here, the actual length of the stems from the ground to the tips is meant rather than the vertical distance of the topmost branches from the ground. This distinction is necessary because many of the branches droop or grow at an angle. The spread of the plant,—that is, the distance around,—is largely dependent upon the angles at which the branches are growing and on the number of stems of the plant. The height of the plant and the number of stems, therefore, are the two distinguishing features as regards size. These

indicate, also, the relative health and vigor of the plant. An attempt was made to differentiate between various types of leaves, with reference to size and color, and between different types as regards blooming and fruiting tendencies. It was found difficult, however, to find individuals which conformed definitely to any particular type. Where certain characteristics existed they were not, as a rule, general over the entire plant, but were usually found on only one side or on only certain stems. Thus, in some cases, one or two stems of a plant bore what appeared to be leaves of a larger size than usual and of a different shade of green, while the remainder of the plant was in every respect like most of the other plants. The same would be true of the number of flowers and berries. In such cases it could not be assumed that the plant represented any special type. It was also noticed that some of these distinctive features were subject to gradual changes, so that their distinctiveness was soon lost.

While the number of plants that have been under observation was probably not sufficiently large to show conclusively that there is no definite correlation between physical appearance and active medicinal properties in the leaves, yet from the data at hand such a condition is at least indicated. Henderson,[5] in commenting on the great variation in the alkaloidal content of different lots of belladonna roots, points out that appearance is no criterion of the quality, the best-appearing roots being often the poorest in medicinal value.

A few actual examples of the lack of relationship between the size of the plant and the alkaloidal content of its leaves may be of interest. The height and spread of all the plants was noted, and it was found that in 1910 plant No. 10, which was the largest in the list, was 42 inches in height and had a spread of 3½ by 4½ feet, yet it contained only 0.536 per cent. alkaloids, a trifle less than the average of all the plants. On the other hand, plant No. 8, which was only half as high and much smaller in spread, showed 0.657 per cent. of alkaloids in its leaves. Again, in 1911, plant No. 15 was the largest plant in the plot as regards height, yet its leaves contained only 0.494 per cent. of alkaloids. The same is true of plants Nos, 4, 43, 45, and 46, while, on the other hand, the leaves of the comparatively small plants, Nos. 21, 29, and 1w, contained 0.630, 0.756, and 0.682 per cent. of alkaloids respectively. In the following year these same plants failed again

[5] Henderson, H. J., "Percentage of Alkaloids in Belladonna Root," *Pharm. Journ.*, vol. 75, No. 3485 (Ser. 4, vol. 21, No. 1832), p. 191, 1905.

to compare favorably with others as regards size, yet the percentages of active constituents in their leaves stood out prominently above the average. There were, however, some plants larger and more vigorous than the average which also contained above the average percentage of alkaloids. The lack of correlation is therefore evident.

Variation Among Individual Plants.

The most important fact established thus far is the great variation in the quantity of alkaloids found in the leaves of individual plants. That some variation should exist was to be expected, since variations are often noted in the chemical constituents of different plants of many species.

To show the great variation found among the comparatively limited number of plants under observation, Table III is presented below.

Table III.

Range of Variation in Percentage of Alkaloids in the Leaves of Belladonna Plants at each Stage of Growth.

Stage of growth	Alkaloidal content of the leaves (per cent.)					
	1910		1911		1912	
	High	Low	High	Low	High	Low
First stage.......	......	......	0.852	0.303	0.869	0.404
Second stage.....	0.700	0.334	.879	.262	.747	.292
Third stage......	......	......	.925	.277	.882	.328
Fourth stage.....	......	......	.891	.311	.806	.359
Fifth stage.......	......	......	.733	.200	.678	.296
Season average.	......	......	.766	.306	.768	.353
Average.......	......	......	.841	.277	.792	.339

From this tabulation it appears that the active principle is more than three times as great in the leaves of some plants than in those of others at the same period of growth, although the plants are in the same plat and therefore grow practically in the same soil and under the same climatic conditions. Under such circumstances the existing variation can hardly be attributed to anything but the inherent characteristic of the individual plant. Much has been written concerning

the influence of soil and climate on the formation of alkaloids in the plants. Gerrard[6] has found that a chalky soil favors the formation of atropin. Chevalier[7] concludes, from his experiments with fertilizers, that the alkaloidal content of certain Solanaceæ can be increased by means of nitrates and farmyard manures. Ransom and Henderson,[8] however, who are working along the line of Chevalier's experiment, have not found thus far that artificial manures materially affect the percentage of alkaloids in the dried leaf, but note in several cases a large increase in the yield of the green plant per acre. Carr[9] claims to have found a certain relationship between the amount of sunshine during the growth of the plant and the percentage of alkaloids found in the stems and leaves, claiming that plenty of sunshine and limited rainfall have a tendency to stimulate the production of alkaloids.

Although soil and climate may have considerable influence on the alkaloidal content of plants, yet to establish this as a fact beyond all doubt is a difficult matter because of the individual variation involved. Until experiments have been conducted upon a large number of plants which show a minimum variation in their alkaloidal content, nothing definite can be said upon this point. In working with a limited number of plants collectively, an abnormally low or high percentage of alkaloids in the leaves of a few might so affect the yield as to make the average entirely misleading. Likewise, this individual variation becomes an important matter in the sampling of large quantities of leaves and roots. In order to secure a reliable sample, it should be of considerable size and selected only after the leaves or roots have been thoroughly mixed.

The existence of great variations in individual plants having been established, the next question was whether such variations existed during only one growing season or manifested themselves in follow-

---

[6] Gerrard, A. W., "On the Alkaloidal Value of Belladonna Plants at Different Periods of Growth," *Yearbook of Pharmacy*, 1881–1882, pp. 400–404, 1882.

[7] Chevalier, J., "Influence de la culture sur la teneur en alcaloides de quelques Solanées," *Compt. Rend. Acad. Sci.* (Paris), T. 150, pp. 344–346, 1910.

[8] Ransom, Francis, and Henderson, H. J., "Belladonna: the Effect of Cultivation and Fertilizers on the Growth of the Plant and Its Alkaloidal Content," *Chemist and Druggist*, vol. 81, No. 1703, pp. 53–55, 1912.

[9] Carr, F. H., "The Effect of Cultivation upon the Alkaloidal Content of Atropa Belladonna," *Chemist and Druggist*, vol. 81, No. 1703, pp. 42–44, 1912.

ing seasons. If plants which are rich in alkaloids one season are correspondingly poor the following season, then it is logical to assume that the production of alkaloids in the plant is dependent on factors which change from year to year. If it were definitely known what rôle the alkaloids play in the metabolism of the plant, it might be easier to determine what factors influence their development. As has been shown, the physical appearance, or, in other words, the

TABLE IV.

Percentage of Alkaloids Above and Below the Average † in the Leaves of Individual Belladonna Plants at Arlington, Va., in 1911 and 1912.

[The figures given are based on the season averages of all the pickings. In each of the 40 plants designated by a star (*) the percentage of alkaloids above or below the average of the entire lot in 1911 varies by not more than one-tenth of 1 per cent. from that in 1912.]

Plant No.	Alkaloids above (+) or below (−) the average (per cent.)		Plant No.	Alkaloids above (+) or below (−) the average (per cent.)	
	1911	1912		1911	1912
1	+0.223	−0.044	31	−0.068	......
2	+ .179	+ .023	32*	− .006	−0.003
3*	− .125	− .116	33*	− .046	+ .044
4*	− .014	+ .014	34*	− .118	− .139
5	+ .047	− .071	35	− .102	+ .071
6*	− .008	− .073	36*	− .086	− .062
7	+ .070	− .081	37*	− .017	+ .003
8*	+ .064	+ .144	38*	+ .063	+ .061
9	+ .048	− .116	39*	− .141	− .072
10*	− .029	− .125	40*	+ .028	− .012
11	+ .087	− .055	41*	− .104	− .076
12*	+ .109	+ .093	42	+ .001	+ .134
13	+ .107	− .023	43*	− .033	− .012
14*	− .044	− .125	44*	− .043	− .082
15*	− .038	+ .005	45*	− .044	− .085
16*	+ .077	+ .086	46*	− .142	− .139
17	− .059	+ .066	47*	− .079	− .040
18*	+ .019	− .011	48	+ .036	− .093
19*	− .005	− .059	49*	+ .024	− .064
20*	+ .036	+ .133	50	− .005	− .192
21*	+ .098	+ .199	1w*	+ .150	+ .174
22	− .078	+ .041	2w*	− .001	+ .015
23*	− .129	− .144	5w*	+ .052	+ .081
24	− .162	......	6w*	+ .234	+ .243
25	− .226	− .056	7w*	+ .172	+ .127
26	+ .035	+ .181	8w	+ .045	− .077
27	− .090	+ .111	9w*	− .018	− .004
28*	− .019	+ .027	10w*	+ .055	+ .065
29*	+ .224	+ .159	11w*	− .088	− .001
30*	− .002	+ .027			

† Average for 1911, 0.532 per cent.; for 1912, 0.545 per cent.

vitality and growing power, of the plant appears to bear no definite relation to the development of alkaloids. Furthermore, if soil and climate are the potent factors, then their influence ought to be felt by all plants alike when all are grown on similar soil and in the same locality. Such, however, has been found not to be the case, and reference to the tables shows that there were plants rich and poor in alkaloids in every year during which the observations extended. On the other hand, if a plant with leaves containing an unusually high or low percentage of alkaloids in one season shows the same characteristics in following years, it is safe to assume that there is a definite tendency in that plant to produce a small or a large quantity of alkaloids in the course of a season's growth, just as in other plants there are well-defined tendencies toward physical characteristics. In order to show the extent to which the characteristic of each plant manifests itself through a number of seasons the following table is presented.

In the plants in Table IV there are a number which are conspicuous because of the high or low percentage of alkaloids in their leaves. Plants Nos. 3, 23, 34, and 46 are, without doubt, greatly

TABLE V.

Alkaloidal Content of the Leaves of Belladonna Plants, Rich and Poor in Alkaloids, at Various Stages of Growth, in 1911 and 1912.

Plant No.	Yield of alkaloids on which selection was based	Alkaloidal content (per cent.)											
		Stage of growth, 1911						Stage of growth, 1912					
		First	Second	Third	Fourth	Fifth	Average	First	Second	Third	Fourth	Fifth	Average
34....	Low.....	0.335	.....	0.526	0.532	0.200	0.414	.....	0.292	0.320	.....	.....	0.406
3.....	Low......	.384	0.375	.277	.549	.451	.407	.....	.393	.448	0.448	.....	.426
23....	Low......	.....	.348	.354	.487	.425	.403	0.496	.366	.341	.....	.....	.401
46....	Low......	.337	.285	.308	.588	.431	.390	.418	.334	.480	.483	0.314	.406
13....	Medium..	.614	.627	.626	.763	.563	.639	.495	.479	.655	.472	.488	.518
12....	High.....	.649	.782	.693	.497	.584	.641	.767	.631	.685	.715	.394	.638
7w....	High.....	.558	.831	.832	.727	.571	.704	.782	.666	.646	.694	.573	.672
6w....	High.....	.596	.879	.925	.711	.722	.766	.847	.747	.882	.804	.558	.768

inferior to the others from a medicinal point of view. On the other hand, Nos. 21, 29, 1w, 6w, and 7w are greatly superior to any others in the list. Furthermore, these plants manifested the same char-

acteristics, not only on the average but at each picking. The recapitulation given in Table V shows this very clearly.

Propagation of the First Generation from Seed of Selected Individuals.

The seed from the individuals selected for exceptionally high and low production of alkaloids were planted in the greenhouse in the following January. After six weeks the young plants were transplanted to two-inch clay pots, and early in May they were set in the field. The seed had been secured during 1911, after the first season's test of the 59 plants had indicated which plants represented the desired type. During the first season these young plants made only sufficient growth to obtain two collective pickings from all the individual plants secured from each selected parent. There were from six to fifteen young plants from the seed of each individual selected. The first picking was secured in July, when the plants were in full bloom, and the second late in August, when the berries were partially ripe. In Table VI the results are summarized.

Table VI.

Alkaloids in the Leaves of First-generation Belladonna Plants Grown from Seed from Selected Parents.

Parent plant		Alkaloidal content (per cent.)			Parent plant		Alkaloidal content (per cent.)		
No.	Yield of alkaloids	First picking	Second picking	Average	No.	Yield of alkaloids	First picking	Second picking	Average
34	Low	0.524	0.693	0.609	12	High	0.650	0.882	0.766
3	Low	.479	.518	.498	7w	High	.617	1.063	.840
13	Medium	.640	.859	.750	6w	High	.805	1.282	1.043

It will be seen that the alkaloidal content of the leaves during this first year indicate that the first-generation plants display the alkaloid-producing characteristic of the parents. Special attention is directed to plants 7w and 6w, the leaves of which contained over 1 per cent. of alkaloids during the second stage. The parents of these plants showed similar superiority over the remainder of the 59 plants originally examined, and there appeared to be no question about the first generation being equally valuable in this respect.

The following year, 1913, these same plants were picked four times: before flowering, when in full bloom, when the berries were

developing, and, finally, when the berries were ripe and much new growth had appeared. The plants were large enough to furnish a sample from each individual. Table VII gives the results from each picking.

TABLE VII.

Alkaloids in the Leaves of Individual First-generation Belladonna Plants at Various Stages of Growth During the Second Season, 1913.

Plant No.	Alkaloidal content (per cent.)				
	First stage, May 5	Second stage, May 23	Third stage, June 21	Fourth stage, Sept. 8	Average for season
34_1	.....	0.316	0.324	.....	0.320
34_2	0.516	.473	.312	0.856	.539
34_3	.608	.....	.352	.863	.604
34_4	.754	.434	.288	.....	.492
34_5	.622	.542	.356	.683	.551
3_1	.538	.366	.430	.523	.466
3_2	.565	.565	.630	.....	.587
3_3	.511	.552	.364	.790	.554
3_4	.693	.607	.350	.833	.621
3_5	.513	.477	.533	.767	.573
3_6	.438	.....	.392	.....	.415
3_7	.412	.415	.504	.....	.444
3_8	.....	.300	.....	.....	.300
3_9	.....	.479	.702	.782	.654
13_1	.....	.255	.459	.934	.549
13_2	.....	.365	.596	.....	.481
13_3	.....	.....	.453	.....	.453
13_4	.492	.359	.318	.649	.455
13_5	.....	.466	.559	.563	.529
13_6	.....	.....	.470	.733	.601
13_7	.....	.341	.552	.766	.553
13_8	.....	.349	.664	.792	.601
13_9	.566	.452	.385	.815	.555
12_1	.854	.653	.737	.494	.688
12_2	.480	.516	.661	.717	.594
12_3	.760	.672	.675	.638	.686
12_4	.605	.572	.626	.....	.619
12_5	.588	.....	.675	.908	.543

Plant No.	Alkaloidal content (per cent.)				
	First stage, May 5	Second stage, May 23	Third stage, June 21	Fourth stage, Sept. 8	Average for season
12_6	0.809	0.601	0.625	0.716	0.688
12_7	.750	.608	.582	.574	.529
12_8	.587	.434	.569	.653	.561
12_9	.....	.....	.389	.549	.469
$7w_1$	.....	.....	.626	.737	.681
$7w_2$	.835	.550	.507	.759	.663
$7w_3$	.620	.563	.431	.782	.599
$7w_4$	.792	.777	.588	.804	.740
$7w_5$	.....	.521	.699	.998	.739
$7w_6$	.674	.721	.567	.663	.656
$7w_7$	.369	.765	.760	.....	.631
$7w_8$	.....	.291	.....	.645	.468
$7w_9$	.714	.389	.544	.....	.412
$7w_{10}$	.634	.496	.489	.764	.596
$7w_{11}$	.....	.404	.626	.773	.601
$6w_1$	.541	.543	.501	.666	.561
$6w_2$	.....	.693	.881	.....	.787
$6w_3$	.850	.641	.787	.885	.791
$6w_4$	.866	.516	.529	.856	.692
$6w_5$	.806	.640	.768	.829	.761
$6w_6$	.780	.735	.663	.733	.728
$6w_7$	.739	.917	1.313	.956	.981
$6w_8$	.780	.921	.937	1.020	.915
$6w_9$	.833	.921	.901	.919	.894
$6w_{10}$	.908	.925	.927	.876	.909
$6w_{11}$	.956	.973	.993	.924	.962
$6w_{12}$	.681	.574	.670	.922	.712
$6w_{13}$	1.143	.639	.852	.754	.847

In order to present the results more clearly the averages of the individuals from each parent are summarized in Table VIII.

TABLE VIII.

Summary of All Individual Plants from Each Parent.

Parent plant		Average alkaloidal content of leaves (per cent.)				
		Stage of growth				Average for season
No.	Yield of alkaloids	First stage	Second stage	Third stage	Fourth stage	
34	Low	0.625	0.441	0.326	0.800	0.501
3	Low	.524	.470	.488	.739	.512
13	Medium	.529	.369	.495	.765	.531
12	High	.679	.573	.617	.662	.597
7w	High	.662	.547	.583	.769	.617
6w	High	.824	.740	.824	.862	.811
Average	......	.640	.523	.555	.766	......

A study of these tables must lead to the conclusion that the first-generation plants have displayed in no small degree the parent characteristic as regards alkaloid production. While from an economic standpoint there is no interest in the low alkaloid-producing plants, they were kept under observation to serve as a means of comparison with the opposite type and to determine whether a low alkaloid production is also an inherent and transmissible characteristic.

STUDIES IN POLLINATION.

Thus far the propagation had been made entirely from seed from cross-pollinated parents. Much experimenting was done in trying to secure close-pollinated seed, with only partial success. The flower of the belladonna plant is so arranged as to make it highly receptive to cross-pollination to such insects as moths, bees, and, especially, bumble-bees. It is questionable whether any appreciable number of flowers become self-pollinated under ordinary conditions. The usual method of bagging was employed the first season, but was a complete failure. The flowers fail to pollinate with their own pollen, the arrangement of anther and stigma reducing the possibility of this to a minimum. As a rule, the flowers withered and dropped off. A further difficulty was experienced in the appearance of aphis in the bags in such numbers as to destroy completely the flower heads enclosed.

The second season the selected plants were screened in by building around them cheese-cloth frames. This method resulted in the pollinating of a few flowers on each plant, but the same difficulty existed. Aphis bred under the shelter in tremendous numbers, and in some cases fumigation with tobacco was necessary. However, sufficient seed was secured to make possible a comparative study of cross- and close-pollination with respect to alkaloid production.

The seed was secured from the original 59 plants. Since some of the selected individuals had died, the test was made with plants 6w and 7w, both selected for high alkaloid-producing tendencies. The seed was sown in the greenhouse and the young plants transplanted to the field in May. Two pickings were secured from all the individuals from each parent from both the cross- and the close-pollinated seed. The first nine samples were picked on August 19, when the plants were flowering, and the second on September 23, when the berries were in various stages of ripeness.

For the sake of brevity, the percentage of alkaloids in the leaves of all the individuals will not be recorded here, but Table IX gives the averages of all individuals from each lot.

TABLE IX.

Average Percentage of Alkaloids in the Leaves of First-generation Belladonna Plants from Seed of Close-pollinated and Cross-pollinated Selected Parents at Two Stages of Growth in 1913.

Lot		Alkaloidal yield of parent	Average alkaloidal content (per cent.)		
No.	Total number of individuals		First stage	Second stage	Season
Lot 6w close-pollinated.....	37	High	0.672	0.701	0.686
Lot 6w cross-pollinated.....	23	High	.586	.602	.594
Lot 7w close-pollinated.....	26	High	.595	.632	.614
Lot 7w cross-pollinated.....	24	High	.618	.611	.615

The following year, 1914, two pickings were again made, and the results for that year are summarized in Table X.

It would appear, from the tables, that the effect of close-pollination as compared with cross-pollination is not so great as would be expected. In the case of 6w the plants from close-pollination are, on the average, 0.092 per cent. richer than those from cross-pollination in 1913, and 0.042 per cent. richer in 1914. The 7w plants show

a difference of 0.001 per cent. in favor of the cross-pollination in 1913 and a difference of 0.062 per cent. in favor of close-pollination in 1914.

TABLE X.

Average Percentage of Alkaloids in the Leaves of First-generation Belladonna Plants from Seed of Close-pollinated and Cross-pollinated Selected Parents at Two Stages of Growth in 1914.

Lot		Alkaloidal yield of parent	Average alkaloidal content (per cent.)		
No.	Total number of individuals		First stage	Second stage	Season
Lot 6w close-pollinated.....	34	High	0.906	0.765	0.835
Lot 6w cross-pollinated.....	19	High	.952	.634	.793
Lot 7w close-pollinated.....	24	High	.855	.753	.804
Lot 7w cross-pollinated.....	27	High	.865	.619	.742

If the results of the above experiment indicate the true value of close-pollination as compared with cross-pollination, the labor and expense necessary to insure close-pollination would seem to make that method of doubtful value. The explanation for the unexpected lack of influence of the close-pollination is not at present apparent.

SECOND-GENERATION PLANTS.

Up to this point the investigation had established the fact that alkaloid production is an inherent characteristic of the plant and can be transmitted to the next generation through seed. It still remained to be found, however, whether such a characteristic could be transmitted to the second and further generations.

For this purpose seed was secured in 1913 from the following first-generation plants: 3_1, 3_6, 3_7, 34_2, 34_3, 34_4, 34_5, 2_2, 2_3, $6w_7$, $6w_{10}$, $6w_{11}$, and $7w_5$. The plants from 3 and 34 were selected as types of low alkaloid-yielding plants, those from 2 as medium, and those from 6w and 7w as types of high alkaloid-yielding types. The seed was planted in the greenhouse at Arlington, Va., in January, 1914, and in May the young seedlings were divided into three lots. One lot was transplanted to the field at Arlington, Va., another was shipped to Timmonsville, S. C., for field transplanting, and the third to Madison, Wis. At Arlington and Madison two pickings were secured, while at Timmonsville only one was secured. Following is the number of individual plants in each lot planted at each of the three locations: $6w_7$, 15; $6w_{10}$, 15; $6w_{11}$, 18; $7w_5$, 4; 2_2, 8; 2_3, 17;

TABLE XI.

Alkaloids in the Leaves of Second-generation Belladonna Plants from Cross-pollinated Parents at Arlington, Va., Madison, Wis., and Timmonsville, S. C., in 1914.

Lot	Production of alkaloids in parent	Alkaloids (per cent.)												
		Arlington, Va.						Madison, Wis.						Timmons-ville, S.C.
		First stage			Second stage			First stage			Second stage			
		Maxi-mum	Mini-mum	Aver-age	Maxi-mum	Mini-mum	Aver-age	Maxi-mum	Mini-mum	Aver-age	Maxi-mum	Mini-mum	Aver-age	Average
$6w_7$	High	0.783	0.414	0.656	0.851	0.340	0.600	1.322	0.478	0.788	1.027	0.461	0.777	0.992
$6w_{10}$	High	.755	.327	.611	.691	.398	.543	1.062	.554	.800	1.115	.557	.829	.906
$6w_{11}$	High	.840	.359	.608	.775	.318	.524	.959	.554	.729	.988	.488	.745	.849
$7w_5$	High	.659	.543	.602	.653	.541	.584	.....	.....	.524	.....	.....	.532	.950
2_2	Medium	.557	.310	.429	.513	.295	.407	1.170	.580	.822	1.221	.605	.840	.....
2_3	Medium	.573	.418	.483	.646	.318	.471	.870	.455	.674	1.309	.366	.814	.771
3_1	Low	.532	.197	.496	.510	.263	.386	.541	.312	.524	.852	.423	.627	.702
3_6	Low	.....	.....	.....	.....	.....	.....	.....	.....	.474	.682	.424	.536	.532
3_7	Low	.502	.412	.446	.636	.318	.421	.717	.488	.602	.978	.630	.722	.669
34_2	Low	.720	.369	.538	.626	.254	.384	.940	.302	.673	.876	.439	.661	.801
34_3	Low	.659	.626	.645	.589	.501	.554	.596	.532	.571	.876	.765	.821	.852
34_4	Low	.641	.398	.496	.593	.142	.414	.471	.346	.530	.756	.478	.660	.663
34_5	Low	.674	.263	.479	.532	.308	.421	.583	.398	.514	.956	.318	.569	.705

3_1, 8; 3_6, 3; 3_7, 10; 34_2, 18; 34_3, 6; 34_4, 13; 34_5, 15. Some of these plants died in transit and in the field, but the number under investigation at Arlington and Madison was approximately that given in the list. At Timmonsville the plants were not picked individually, but one sample was secured from each lot. In Table XI the results of the analyses of these samples are summarized.

In order to show more clearly the rank of the several lots at the different locations, the averages are summarized in Table XII.

TABLE XII.

Averages of all the Plants from Each Parent at all Stages and at all Three Locations.

Parent	Plants included	Nature of alkaloid production	Percentage of alkaloids in leaves		
			Arlington, Va.	Madison, Wis.	Timmonsville, S. C.
6w......	All individual plants of lots $6w_7$, $6w_{10}$, and $6w_{11}$	High	0.592	0.778	0.916
7w......	All individual plants of lot $7w_5$	High	0.593	0.528	0.950
2........	All individual plants of lots 2_2, 2_3	Medium	0.446	0.788	0.771
34.......	All individual plants of lots 34_2, 34_3, 34_4, and 34_5	Low	0.491	0.642	0.755
3........	All individual plants of lots 3_1, 3_6, and 3_7	Low	0.437	0.581	0.634

A study of the averages leads to the conclusion that even at the three widely-separated localities these second-generation plants arrange themselves largely in the same order as the original selected parents. There are some exceptions, it is true. Thus at Madison, Wis., the averages show the plants of 7w to have been much weaker than the medium and low types 2, 34, and 3. However, only two individual plants of this lot lived, and hence the averages in that case are not a safe indication. This is the only notable exception to be found.

When it is considered that we have here plants two generations removed from the selected stock and propagated from cross-pollinated seed, the fact that their alkaloid-producing tendencies still show distinctly the character of the parent must be considered as fairly conclusive evidence of what can be accomplished. When it is further remembered that this last generation was grown in widely-separated localities the extent to which this metabolistic character is transmitted becomes still more evident.

Relation of Soil and Climate to Alkaloid Production.

The growing of belladonna plants from selected seed at the three localities mentioned offered exceptional opportunities to study the influence of soil and climate on alkaloid formation in the plants. This question is far from settled. As has already been mentioned, Gerrard, Chevalier, and Ransom and Henderson have studied the influence of various fertilizers on belladonna, but their conclusions are not entirely in accord. The writer has conducted fertilizer tests for several years, but the results failed to warrant any definite conclusions. Furthermore, such experiments, in view of the great variations found to exist in the alkaloidal content of belladonna plants, are likely to lead to questionable conclusions.

From the rather limited data secured with the second-generation plants one would be led to conclude that at Timmonsville, S. C., the plants find conditions conducive to high alkaloid production. However, since only one picking was secured during the season, such a conclusion is open to question. The soil at Madison, Wis., and at Arlington, Va., is a heavy clay, while at Timmonsville it is very sandy.

What are claimed to be equally important factors are sunshine and rainfall. Carr [10] claims that a maximum of sunshine and minimum of rainfall produces the greatest quantity of alkaloids. According to the records of the Weather Bureau, the total rainfall during May, June, July, and August, 1914, at Arlington, Va., Madison, Wis., and Florence, S. C. (7 miles from Timmonsville), was 16.24, 14.52, and 13.08 inches, respectively. The total number of clear days was 43, 41, and 46 respectively. According to the conclusions of Carr, the conditions at South Carolina should favor the production of the greatest percentage of alkaloids, since it had the least rainfall and the greatest number of clear days, which, of course, means sunshine. It can hardly be concluded, however, that this condition is responsible for the higher averages found at Timmonsville, because the difference in rainfall and clear days is entirely too slight. The writer is inclined to think, however, that an exceptionally dry and hot season will stimulate alkaloidal production. It is true, of course, that in such a season a minimum amount of growth is made by the plant, and it is not improbable that the actual production of alkaloids is normal to the plant and that the total weight is so much smaller that on analysis a greater concentration of alkaloids is indicated. This may

[10] Carr, F. H., *Op. cit.*

also account for the seemingly greater percentage of alkaloids in the leaves in late summer, when the plant has the minimum foliage. Later in the season, when new fall growth appears, the percentage of alkaloids, as a rule, is nearer the average. It is not impossible that it is simply a translocation of constituents, or a crowding, as it were, of such constituents into less space.

Vegetable Propagation.

The question of propagating the desirable types of belladonna plants by vegetative means has also received some consideration. Good cuttings made in fall will take root fairly well in the greenhouse, but careful attention to moisture and temperature is absolutely necessary. By spring such cuttings have made a substantial root growth and can be transplanted to the field with very little loss.

Cuttings were secured from the first-generation plants in the fall of 1913. In 1914 two samples of leaves were secured from the individuals of each lot, which ranged from one to eight in number. For the sake of brevity, the percentage of alkaloids found in each individual will not be given, but in Table XIII the averages are presented.

Table XIII.

Summary of Seasonal and Group Averages of Plants Propagated from Selected Parents.

Lot	Alkaloid yield of parent	Average alkaloidal content (per cent.)	
		For season	For all plants from same parent
Lot $6w_1$	High	0.532	0.616
Lot $6w_2$	High	.517	
Lot $6w_3$	High	.634	
Lot $6w_4$	High	.565	
Lot $6w_8$	High	.772	
Lot $6w_9$	High	.643	
Lot $6w_{10}$	High	.648	
Lot $6w_{11}$	High	.649	
Lot $6w_{12}$	High	.581	
Lot $7w_3$	High	.544	0.610
Lot $7w_4$	High	.575	
Lot $7w_5$	High	.677	
Lot $7w_{10}$	High	.646	
Lot 34_2	Low	.537	0.529
Lot 34_3	Low	.588	
Lot 34_5	Low	.463	

As was to be expected, the cuttings show distinctly the same character as regards alkaloid production as the plants from which they were obtained.

While vegetative means can be employed in propagating desirable types, it is questionable whether the practice is practical as compared with propagation through seed. The cuttings on a commercial scale would require a great deal of space in winter and constant attention, while the seed can be sown in cold frames without attention. Furthermore, from the writer's observation, the cuttings, when set out in the field in spring, although hardy, make comparatively small leaf growth during the season as compared with seedlings. This would, of course, be a distinct disadvantage where tonnage per acre is considered.

Roots.

In this investigation the percentage of alkaloids in the leaves has been used in all cases. It would be of equal interest to study the alkaloids in the roots. The question of variation in the percentage in the roots is as unexplored as was that relating to the leaves when this investigation was undertaken. It would be interesting to know the extent to which high percentage in the leaves is paralleled, if at all, by a similar condition in the roots; also, whether the progeny, either from seed or cuttings, came true to type if the selection were based on the character of the root.

General Considerations.

In presenting the results of this investigation the writer has intended to bring to the notice of pharmacists, pharmaceutical manufacturers, and prospective growers of medicinal plants a subject which should be of interest at a time when the improvement of our drug plants is imperative and when such improvements can be undertaken under the best economic conditions. As has been stated, such work can be successfully undertaken only by special growers who have special training or employ specialists and who have the requisite laboratory facilities. There are no special difficulties connected with the problem. It is no difficult matter for the grower to stake out numerous individual plants in his field, make several analyses of their leaves during the season, and preserve the seed from desirable individuals. The following year this seed will give him a small plot of selected plants, which should preferably be some distance away from the general field. While all the individuals in such a plot will not be

high in akaloids, the great majority are likely to be, and the collective seed from such a plot should yield, the following season, a field of belladonna of superior quality. While, in this investigation, the strain has been maintained through two generations, it will doubtless become weaker through further generations. It would be advisable, no doubt, to make new selections at least every other year in order to keep the quality of the crop from deteriorating.

Belladonna is by no means the only medicinal plant to be considered. It was selected for this work because it was especially suited for such a study, but the Office of Drug-Plant Investigations has already under way similar studies on hyoscyamus and digitalis. In the case of the former, certain cultural difficulties must be overcome first, while digitalis presents a somewhat more difficult problem, in that its active constituents are not as readily nor as accurately measured. However, if it is found that the improvement of belladonna can be successfully undertaken by scientifically-trained drug growers, it should be sufficient encouragement to apply similar methods to a much wider field until the cultivation of medicinal plants in this country is placed on such a basis as to furnish not only quantity but high quality of drugs for domestic use.

NOTE ON TESTING CALCIUM COMPOUNDS.

By Carl E. Smith.

This is written to draw attention to a deficiency in the tests of the United States Pharmacopœia for the identification of calcium compounds and for the detection of certain possible contaminations, such as might easily lead to serious results because of the false sense of security the official tests would give. As an example it might be mentioned that a specimen of strontium carbonate containing several per cent. of barium carbonate will stand all the tests given in the U.S.P. for establishing the identity and purity of precipitated calcium carbonate.

A sample of powder was recently submitted to the writer for analysis, which, because of a statement accompanying it concerning its uses, was supposed to consist, in greater part at least, of calcium salts. Preliminary tests proved presence of alkaline earth carbonate in large quantity. This led to the tentative conclusion that the powder probably consisted chiefly of calcium carbonate, as there was no reason to suspect presence of barium or strontium salts. Absence of color and complete solubility in dilute acids excluded the presence

of elutriated native chalk. It was therefore expected that the U.S.P. tests laid down for precipitated chalk would definitely establish its identity as such and also detect in great probability any impurity or admixture. The sample stood all the tests and conformed also to the description of physical properties given. A little sodium chloride and traces of iron were found and as the U.S.P. lacks a test for magnesia, which is often found in calcium salts to some extent, a test was made in the usual way with phosphate, and a reaction was obtained that apparently indicated the presence of a small amount of that impurity. Dependence on the U.S.P. tests, therefore, would have led to the conclusion that the specimen in question not only was calcium carbonate, but a salt of such a degree of purity as to warrant its use in medicinal preparations. Further examination, however, showed that the sample was *not* calcium carbonate, that it contained neither calcium nor magnesium, but consisted of strontium carbonate contaminated with about 1.5 per cent. of barium carbonate.

The test upon which the Pharmacopœia relies entirely for the identification of calcium salts is the production of a precipitate on addition, to the neutral solution, of a solution of ammonium oxalate, said precipitate to be soluble in hydrochloric acid, but insoluble in acetic acid. But this reaction is by no means characteristic of calcium alone. It is shared by strontium and, to some extent, by barium, and neither of these latter is excluded or detected by any other test provided. It is true that calcium salts are not liable to contain either barium or strontium as natural impurities, nor are they liable to be introduced in the course of manufacture, but accidental substitution or admixture might readily take place and such contingencies should certainly be guarded against by suitable means.

Examination of the text of the U.S.P. pertaining to other calcium salts shows that in no case do the tests adequately differentiate calcium from other alkaline earth compounds. A test for the identification of a substance should be characteristic enough to distinguish it from everything else, beyond all reasonable doubt.

Of course, the remedy for the defects pointed out in this note is self-evident to every competent analyst. It need only be mentioned that a saturated water solution of calcium sulphate would seem to be the simplest means of detecting the presence of either barium or strontium.

Carl E. Smith Testing and Research Laboratory,
5 Beekman Street, New York.

EXPERIMENTAL DEMONSTRATIONS OF ADHESION ALKALOIDAL REACTIONS.*

By John Uri Lloyd, Ph.M.

The speaker was introduced by Professor J. P. Remington, who happily referred to Mr. Lloyd's lifetime devoted to such studies as were to be the feature of the present meeting. His remarks, in recognition of the research accomplishments of their guest, were highly complimentary. Indeed, he added, his long established contributions had led the Philadelphia College of Pharmacy, as early as 1890, to confer upon him the degree of Ph.M. "Therefore," said Professor Remington, "we to-day welcome one of our own members to his Philadelphia home, and shall listen with interest to the message he brings to us in this exhibition phase of one of the features of a life-work devoted to patient pharmaceutical research."

Professor Lloyd prefaced his remarks by asking that the experimental phenomena presented be accepted as established facts, but that his cautiously offered explanations therefor be considered as opinions merely based on his present knowledge. He claimed the privilege of revising his views of the reactions in accordance with evidence presented hereafter by either other investigators or himself. "This is a nearly untrodden field," he said, "and needs now be cautiously touched, theoretically."

Continuing, Professor Lloyd said, "I consider the process to be that of *adhesion,* but if this be true, a phase of the reaction with the alkaloids of sanguinaria is exceedingly puzzling, as indicated in my paper presented to the recent meeting of the American Pharmaceutical Association, San Francisco. *'Adhesion'* is, however, the best term now in view, and receives the support of such eminent scientists as Ostwald and Gordin."

The alkaloidal reagent employed by Professor Lloyd is a highly hydrated condition of aluminum silicate, in exceeding colloidal form. He explained the process of its production from plastic clay or fuller's earth, and ventured to predict that it might yet be demonstrated that to the *water* side of the compound might be attributed its attractive energy. "Almost I would venture to coin for the most potent form of this reagent the term 'Colloidal Water,'" he said. Then he added, "At least, the alkaloidal affinity depends on the

* Address delivered at a Pharmaceutical Meeting on March 24, 1916.

influence of the water present, because *anhydrous* aluminum silicate has no alkaloidal attraction whatever."

" The term *colloidal,"* he said, " is used after the general definition of Graham, but I might perhaps as well, or even better, employ the term *amorphous*. Indeed, in the series of pharmacy articles contributed to the American Pharmaceutical Association, 1879 to 1885, I used the terms, 'mass action,' 'structural affinity,' 'amorphous' and 'colloidal.' Possibly I can no better now, than then, differentiate between these terms.

" The reagent is without crystalline form, and so are the alkaloids I have thus far abstracted by it, with one exception. This alkaloid I call the *'Second Alkaloid of Veratrum.'* And yet, under certain artificial strains, crystals can be produced from the amorphous forms of some of the others." This point was later illustrated on the screen.

These prefatory remarks, the speaker stated, were designed to enable him to introduce, as intelligently as possible, the experiments to follow, and he added that he again claimed the privilege of revising his present views concerning any theoretical phase of the problem.

He then dissolved bisulphate of quinine in a large cylinder of water, made the solution acid with sulphuric acid, and next divided it into two portions. To one he added a small amount of his reagent, and having shaken it well, filtered it into a cylinder, which he placed beside the reserved half. The original was deeply fluorescent, the filtered part devoid of fluorescence. Then to each he added Mayer's test solution for alkaloids. An abundant precipitate occurred in the original. The filtrate from the portion acted upon by the reagent remained transparent.

He now mixed a portion of high-grade alkaloidal, powdered cinchona bark, with dilute sulphuric acid and filtered. To one-half of the filtrate he added a portion of his reagent and filtered it into a cylinder beside the reserved portion. Then to each he added Mayer's test reagent. The original gave a heavy white precipitate. None whatever occurred in the other.

Said he, " Nature has fortunately given us two alkaloids that yield colored salts, one yellow (berberine), the other red (sanguinarine)." He dissolved, separately, berberine sulphate and sanguinarine sulphate, dividing each liquid into two parts. To one part of each he added a portion of his reagent, filtering into a cylinder beside the reserved, *colored* half. *Both filtrates passed transparent, and as colorless as water.* These experiments were very striking.

"May I venture to ask the privilege of voicing my conclusions concerning certain phases of this phenomenon?" asked the speaker.

"This reagent is a colloidal form of hydrous aluminum silicate, and is insoluble in water. It is so nearly neutral as scarcely to affect either red or blue litmus paper. And yet, it has the power of grasping an alkaloid or its salt, or a natural texture of alkaloidal relationship in which an alkaloid resides, even though the alkaloidal part be in almost inappreciable amount. Seemingly, the colloidal sponge sucks bodily the alkaloid or alkaloid-bearing texture into itself. *This, in the presence of an acid,* the usual solvent of alkaloids.

"I consider the water-saturated, colloidal reagent to be made up of a magma comprising groups of *Colloidal Sponges,* in varying conditions of hydration, in which, perhaps, the earthy particles are mere microscopic points that are held apart by water zones and surface films. Perhaps the entire corpuscle is an adhesion compound in which earth and water are blended into a complex whole. The energy of the compound depends on the *colloidal condition* of the structure, and is governed by the condition and proportions of the water of adhesion. The addition of the alkaloid to the reagent liberates this water and destroys the colloidal condition of the mother sponge, the product which, before, was a slime, settling as earth does in water.

"So tenaciously are the alkaloids held by this reagent that even strychnine is no longer bitter. And yet, the combination has been shown to be as active, physiologically, as the ordinary alkaloidal salts of strychnine. Other bitter alkaloids, such as berberine, are likewise tasteless, but some alkaloids leave a lingering after-taste of bitterness, due to the alkaline nature of the saliva, which, dissociating the compound, liberates traces of the alkaloid.

"This liberation of the alkaloid by an alkali may be advantageously utilized in alkaloidal manipulations. From a drug percolated with dilute acid, or even by water, the alkaloid may be separated by means of the reagent, and from this combination liberated by means of an alkali in the presence of a suitable solvent, such as chloroform or ether, from which it may be recovered, by usual processes."

Notwithstanding that the alkaloids thus obtained are amorphous or colloidal, they may, under artificial strain, assume crystalline conditions.

This was illustrated by a series of graphic slide presentations in

which the reagent was first shown as colloidal globules which, when alkaloid saturated, still remained colloidal, but when in thin film, the alkaloid was liberated, it formed micro-crystals that, with the specimens illustrated (strychnine and cocaine), were very characteristic. As a final suggestion, attention was called to the fact that in their natural settings the alkaloidal textures of green drugs were colloidal, be they juice or tissue.

After the exhibition, a call was made on Professor Kraemer, whose accomplishments in botany and in plant histology eminently fitted him to make a balanced review of the lesson of the day. His comments were addressed mainly to the students of the College of Pharmacy present, and were of such a nature as to inspire them with their opportunities. Said he, "It can be seen that even a neglected earth may yield a substance that may open the door to a new study of plant structures. These beautiful experiments, and these attractive screen illustrations, are due, not to stumbling accidents, but are the result of a lifetime of persevering study, but for which the discovery would not have been made, and the phenomena presented would have been unnoticed." Professor Kraemer begged the audience to take the lesson as an inspiration. "Indeed," he added, "I am not so sure but that Professor Lloyd has brought to us this exhibition for the purpose of opening avenues of investigation, both practical and theoretical."

THE "NOBLE" GASES.

How the "Nitrogen" of a Generation Ago Has Been Made to Yield Six, and Possibly Seven, Elements and the Value of This Discovery to Chemistry.[1]

By Henry P. Talbot.

From the earliest days of quantitative chemical experimentation the atmosphere has been the subject of frequent investigation. The discovery of oxygen as a separate entity resulted from the independent researches of Priestley in England and Scheele in Sweden about 1774, and nitrogen had been recognized as a new gaseous substance by Rutherford in 1772. The part which these two gases play in the atmosphere was demonstrated a little later, and for more than a

[1] Reprinted from *Science Conspectus*, 1916, p. 16.

century the literature contains innumerable records of physical and chemical measurements based upon the assumption that these two elements constitute the sole essential constituents of the gaseous envelope of the earth. Other substances, such as moisture, ammonia, and carbon dioxide, are, to be sure, universally present, but are accidental components, varying in amount according to local conditions, while oxygen and nitrogen are to be found in approximately constant proportions, no matter where the specimens of air may be collected.

Such was the universal belief when, in 1893, Lord Rayleigh, an English physicist, undertook to review the measurements of some of the natural constants of the more common permanent gases, among them the density of nitrogen gas. He was profoundly astonished to discover that "nitrogen" obtained from the atmosphere after removal of the other constituents, according to the then accepted methods, was distinctly heavier, volume for volume, than nitrogen obtained from the decomposition of chemical compounds of which it is a component. The differences were much too large to be accounted for by errors in manipulation or observation, since these were accurate to about one part in ten thousand, while the discrepancies in weight were of the order of one part in two thousand.

When this announcement was made public, speculation as to the cause of the observed difference in density was rife, but it soon became highly probable that a search must be made for a new element in "atmospheric nitrogen," as the residual gas which remains after the removal of the other constituents from the atmosphere is now called. To this search Lord Rayleigh and Professor (now Sir William) Ramsay addressed themselves.

They first employed a method which was a repetition of work done nearly a century before by Cavendish. An electric discharge was passed through air in the presence of an alkali. This causes the oxygen to combine with a part of the nitrogen and the products of the combustion are absorbed by the alkali. In this way the oxygen can be removed, and the residue is "atmospheric nitrogen." Nitrogen is a comparatively inactive element in a chemical sense, but it can be made to combine directly with certain of the metals, such as magnesium, and by repeatedly passing the residual gas over the metal until no more diminution in volume occurred, they obtained a small quantity of a gas which was twenty times as heavy as hydrogen (taken as a standard), whereas nitrogen is only fourteen times as

heavy. This final residual gas was found to amount to a little less than 1 per cent. by volume of the original air. These results were confirmed by other and different procedures, and in 1895 the two co-workers felt justified in announcing the discovery of a new element, to which they gave the name argon, the inert; a name which later investigation has justified, since argon has resisted all attempts of the most varied character to induce it to enter into chemical combination with any of the other elements.

It is interesting to note that Cavendish just missed the discovery of this element, for in the record of his experiments we find that, when sparking a mixture of nitrogen with an excess of oxygen, he obtained a residue, of which he says: "If there is any part of the phlogisticated air (now called nitrogen) of our atmosphere which differs from the rest and cannot be reduced to nitrous acid, we may safely conclude that it is not more than one-one hundred and twentieth of the whole." The residue was undoubtedly argon, and it is remarkable that this record should have passed unnoticed for more than a century.

The chemist conceives that any given element is not indefinitely subdivisible by chemical agencies. He terms the ultimate particles atoms and further conceives that compounds are formed by the union of atoms of different elements. It is not possible to determine with accuracy the absolute weights of these atoms in terms of any units of weight in common use, but it is possible to determine the relative weights of the atoms of different elements, in terms of the weight of the atom of hydrogen taken as a standard. When a new element is discovered, almost the first concern of the chemist is to fix a value for its atomic weight on this hydrogen scale. Although argon, as already stated, forms no chemical compounds, it was found possible from its physical constants to fix upon a value for its atomic weight with much probability of truth. But a fresh difficulty then presented itself; namely, that this new element did not fit into the so-called periodic system of the elements. Mendelejeff has found that, if the known elements are arranged in the order of their atomic weights, those elements which have generally similar properties recur periodically in the resulting system. But argon, with an atomic weight 40, which was the value found for it, would be out of place; that is, it would be associated in the system with very dissimilar elements. Since repeated determinations of the atomic weight made upon different specimens of the gas confirmed the figures first obtained, and since,

according to the periodic system, the value seemed to be too large, a search was begun for possible small admixtures with the argon of a second new element with larger atomic weight.

At this time it was recalled that nitrogen had been found in the gases occluded in certain minerals, and it was suggested that argon might also be found in these gases. Professor Ramsay collected a considerable quantity of the gases from a mineral called cleveite, and these did contain argon, but they yielded also another new element, although not the one for which they were searching. In this discovery the spectroscope played the principal part. It is known that highly heated gases give out light which when examined with the aid of a prism is found to be different from sunlight, in that it does not produce a continuous spectrum. The heated gases emit light of certain definite wave-lengths, which appear as bright lines in different parts of the spectrum. These lines can be charted with great exactness and have a constant position for a given element. Sir William Crookes, who made the spectroscopic examination of the gases from cleveite, reported the presence of an element yielding lines identical with those shown in the spectrum of the sun's chromosphere during an eclipse, and ascribed as far back as 1868, by Lockyer, to an element which he called helium. Later measurements confirmed the identity of the lines in the spectrum of the new gas with those of helium, and density determinations showed that this element has an atomic weight of 4 on the scale indicated above. It could not, therefore, account for the discrepancy in the atomic weight of argon, but its discovery clearly pointed to the existence of other elements of the general character of argon. It should be noted in passing that the similarity of the spectra of argon and nitrogen, as well as its inert character, largely accounts for the failure to detect its presence in the atmosphere for so long a time.

Thus stimulated, the search for other inactive elements was continued. A considerable quantity of argon from the atmosphere had been laboriously collected, and preparations were made to liquefy it and subject the liquid to fractional distillation; that is, to allow it to evaporate slowly, collecting the gases evolved in separate portions or "fractions," the first of which would contain a larger proportion of that element which boiled away most readily, just as alcohol tends to boil away first from a mixture of alcohol and water in the radiator of an automobile. These "fractions" were then separately liquefied, and each, in turn, refractionated, in this way gradually separating

the more volatile from the less volatile constituents. The same procedure was applied to the residues obtained upon the evaporation of liquid air. Indeed, without the use of liquid air and liquid hydrogen, as refrigerating agents, or the skill in manipulation of liquefied gases obtained through the handling of liquid air, together with the perfection of the evacuated double-walled Dewar flasks, the isolation of the different inert gases would not have been possible.

The separation by means of fractional distillation had to be supplemented by other physical methods, namely, atmolysis, or diffusion through minute openings; and later, the adsorption of gases in the pores of willow-charcoal at low temperatures. The less the density of a gas the more readily it diffuses, hence by passing a mixture of gases of different densities through something like the stem of a clay pipe, the lighter gas is made to pass through the pores at a more rapid rate than the others and may be collected from the outside.

By combinations of these three procedures, fractional distillation, diffusion, and selective adsorption in charcoal, it has been possible to isolate and identify five members of this wholly unique group of gases, often called the "noble gases" because of their apparent disinclination to associate themselves with other elements. The elements are helium, neon, argon, krypton, and xenon. The first two are lighter, the last two heavier, than argon. Notwithstanding the discovery of the two latter elements, the anomalous position of argon in the periodic system is still unexplained, since they are not present in sufficient amounts to alter appreciably the atomic weight determination. The other members fit into the periodic system without difficulty.

A sixth member has recently been added to the group in the discovery of niton, the emanation given off by radium compounds in the first step of their disintegration. This has been obtained in amounts weighable only by specially constructed balances of remarkable accuracy, but, notwithstanding the great difficulties to be overcome, its atomic weight has been determined with probable accuracy, and its chemical inertness established. There is some reason for suspecting the existence of a seventh "noble gas," lighter than helium, which, because of its small mass, would not probably remain in the earth's atmosphere but would be attracted by the larger heavenly bodies, and would even then probably be found only in the outer portions of their atmosphere. Spectral lines have been detected from the sun's corona, emitted by some substance outside the zone of hydrogen or helium, and these lines are not identical with

those of any terrestrially known element. The name coronium has been tentatively assigned to this element—just as helium was named by Lockyer in 1868—and it may be another " noble " gas.

Five members of this group, helium, neon, argon, krypton, and xenon, are found in the atmosphere, and niton is probably present in most minute amounts. The proportions of the other gases seem to be about as follows:

Helium, 1 : 185,000; neon, 1 : 55,000; argon, 1 : 160.3; krypton, 1 : 20,000,000; xenon, 1 : 170,000,000.

Liquid air is the source of all of these gases to-day, except helium, which although present in liquid air is more readily obtained from the gases occluded in certain minerals, as noted already. Neon has offered the greatest difficulties in purification.

The discovery of a series of elements without any chemistry, such as had been unknown and possibly unimagined, was, of course, sufficient to excite great scientific interest, after a certain period of incredulity as to the validity of the discovery had passed. Their scientific importance is further enormously enhanced by the discovery that helium is a product of the disintegration of radioactive materials, and that all terrestrial helium probably owes its origin to this source. There is no direct evidence at present that any of the other inert gases, except niton, have a similar origin, but the final conclusion on this point has yet to be reached.

Helium remained unique for some time after its discovery as the only gas which it was impossible to liquefy. Even Dewar, so skilled in such methods, was unsuccessful, but Onnes, building upon the foundation laid by Dewar, has succeeded, and has produced liquid helium in considerable quantities. Its boiling-point is about 4° above absolute zero, that is, about $-269°$ C., and Professor Onnes has conducted a series of most valuable investigations upon the effect of this temperature (the lowest at our command) upon physical phenomena, notably electrical phenomena. One of the most striking results of his investigations is his demonstration that an electrical current induced in a lead ring placed in liquid helium continues to flow for a long time after the exciting cause is removed; that is, electrical resistance nearly disappears at that temperature. It is evident that this opens an immense field for experimentation and speculation.

Argon is now comparatively easily obtainable from liquid air, provided it is not necessary to purify it from the small amounts of

the other inert gases, which do no harm in argon for technical purposes. It has already found commercial use in the "argon lamp," the successor of the nitrogen lamp. Formerly the bulbs of the tungsten lamps were evacuated as completely as possible, but it was subsequently found that if these lamps were filled with nitrogen at atmospheric pressure they could be run at a higher temperature and greater efficiency without too great evaporation of tungsten from the filaments. This is supposed to be due, in part, to the collision of the molecules of tungsten as they leave the surface of the filament with those of nitrogen gas, which drives many of them back to the filament. Since argon has a heavier molecule than nitrogen, and is completely inert, it has been substituted in these lamps, with a resulting further increase in efficiency.

Krypton, notwithstanding the minute proportions in the atmosphere, is possibly intimately connected with the phenomena of "northern lights," since the spectrum of these lights shows the lines of krypton with considerable prominence.

From a scientific viewpoint niton is the most unusual of these elements, since it possesses two characteristics which were absolutely unknown in 1895; namely, complete chemical inactivity, and a temporary existence due to atomic disintegration, the discovery of which has given rise to a new primary science, radioactivity. Niton has already been used, in aqueous solution, as a curative agent in radiotherapy. The nature of the changes involved could not be made clear without a somewhat extensive presentation of radioactive phenomena in general.

Although of comparatively little practical value in themselves, the discovery of these noble gases, closely associated as two of them are known to be with the story of radium and its congeners, has had an enormous influence upon our present concepts in physics and chemistry which is daily bearing fruit. What the future may bring is beyond the compass of our imaginations, but new ground has been broken, which has permitted us to delve a little deeper into the foundations of scientific knowledge. Old concepts have been confirmed and broadened (very few destroyed), while vast unsuspected stores of energy in common matter have been revealed, which only our ignorance of to-day prevents us from using for the purposes of life.

BOOK REVIEWS.

New and Non-official Remedies, 1916, Containing Descriptions of the Articles Which Have Been Accepted by the Council on Pharmacy and Chemistry of the American Medical Association Prior to January 1, 1916. This book, which makes its appearance annually, carefully revised and up-to-date, is beginning to assume almost voluminous proportions. Including the usual index and an index to distributers, it consists of 428 pages of information concerning newer remedies and the latest knowledge concerning the remedies that have been known to medical science for decades. For illustration, nearly twelve pages are devoted to "digitalis principles and preparations," and give, in a clear and succinct manner, all the information about the cardiac tonics that the busy practitioner should know. Under "Arsenic and Arsenic Compounds," much valuable information is given pertaining to the latest organic combinations of this important drug. Several pages are devoted to Ehrlich's Salvarsan and Neosalvarsan and information of a kind given that the pharmacist may be called upon to make use of at any time in serving his medical clientèle. Much information of a practical nature is given concerning serums and vaccines, diagnostic agents, antigens used for prophylactic or therapeutic purposes, radium and radium salts, and not the least valuable part of this book is the information as to where these things are obtainable; who manufactures and distributes; where a medicinal preparation is manufactured and how readily it can be obtained are many times matters of great importance to the busy physician and pharmacist. The so-called digestive ferments are also considered and the various organs of animals used in therapeutics are commented on. The Council, however, states that it assumes no responsibility for the quality or identity of preparations from the latter. Lactic-acid producing organisms and preparations are briefly reviewed and discussed from the viewpoint of common sense.

John K. Thum.

Digest of Comments on the Pharmacopœia of the United States of America and the National Formulary for the Calendar Year Ending December 31, 1914, by Martin I. Wilbert, Hygienic Laboratory Bulletin No. 105, February, 1916, Washington, Government Printing Office. The present volume, like those that have been published before it, contains much interesting matter in

the way of brief references anent pharmacopœial literature. A list of the publications reviewed is given and is striking evidence of the painstaking efforts made to cover all of the available literature bearing on pharmacopœial revision. Of course, in a work of this kind the references must necessarily be of a brief nature, and this point is conceded by the author. Despite that fact, the information and suggestions one sees throughout the book prove its usefulness. That it has been of considerable benefit to those who are directly interested in the work of revising the U.S.P. and the N.F. must be apparent to all those who know what revision work means. A. Tschirch, in a paper published in 1913, tersely remarks that successful revision is dependent on a "complete and perfect review of the literature pertaining to pharmacy and materia medica." And he goes on to say that "the practical Americans have long been aware of this part of pharmacopœial revision and have taken means to overcome it" by governmental publication of references to articles bearing on this important work. While Tschirch's paper deals altogether with the subject of establishing an international pharmacopœial bureau, his remark that abstracting activity should be supplemented with the findings from a central laboratory will, no doubt, appeal to many as being applicable to furthering and broadening the activity of the "Digest."

Including the index, this volume consists of nearly 509 pages. Abstracts referring to articles on foreign pharmacopœias and international standards are also given and should prove of much practical value.

JOHN K. THUM.

PHILADELPHIA COLLEGE OF PHARMACY.

ANNUAL MEETING.

The annual meeting of the Philadelphia College of Pharmacy was held March 27, 1916, at 4 P.M., in the Library, the President, Howard B. French, presiding. Nineteen members were present. The minutes of the quarterly meeting, held December 27, 1915, were read and approved. The minutes of the Board of Trustees for December, 1915, January and February, 1916, were read by the Registrar, J. S. Beetem, and approved.

President French then delivered his annual address, at the conclusion of which considerable applause was given, when, on motion,

duly seconded, the address was referred to the Committee of Publication with leave to abstract.

REPORT OF COMMITTEE OF PUBLICATION.—In the absence of the chairman, Professor Sadtler, the report was read by Professor Remington. "THE AMERICAN JOURNAL OF PHARMACY has been published regularly during the past twelve months. The financial statement herewith presented covers the period from March 17, 1915, to March 15, 1916. All bills having been paid, the financial report is very gratifying to the Committee in that it shows a balance which is twice that of last year. The receipts from subscriptions and sale of back numbers exceed all previous records. The question of supplying back numbers is giving us much concern, and if our members would keep on the lookout for back numbers, especially the earlier volumes, it would help us very much. The Committee record their appreciation of the interest of the Massachusetts College of Pharmacy and our fellow-members, Mr. Beringer and Mr. Beetem, in sending a supply of back numbers. The usual annual appropriation from the College to pay for cost of copies to members and exchanges was made."

REPORT OF THE EDITOR.—Professor Henry Kraemer said:

"Such things as the Atlantic Monthly," wrote Charles Eliot Norton to James Russell Lowell in 1857, "are never permanent in our country. They burn brightly for a little while and then burn out and some other light takes their place. It would be a great thing for us if any undertaking of this kind could live long enough to get affections and associations connected with it whose steady glow should take the place and more than supply the shine of novelty and the dazzle of a first go-off." Fortunately there has been a culture and a scholarship developed in this country to support the Atlantic Monthly, and this magazine of three generations is one of the proudest possessions of the American people. If we revert back to the beginnings of our JOURNAL in 1825, it will be apparent that the College was not only ambitious, but that the members had a faith greater than that of Norton when the Atlantic Monthly was founded. The first four numbers were published on December, 1825, May, 1826, September, 1827, and November, 1827. In these numbers we find special papers by Daniel B. Smith, Samuel Jackson, R. A. Hare, and others. These numbers were published by the Publishing Committee, consisting of Samuel Jackson, M.D., Henry Troth, Solomon Temple, Ellis H. Yarnall, and Daniel B. Smith.

In 1829, largely due to the efforts of Dr. Benjamin Ellis, the JOURNAL was launched with a definite policy and the regular volumes were begun. He was assisted by the Publishing Committee, consisting of Daniel B. Smith, Charles Ellis, S. P. Griffitts, Jr., and Dr. George B. Wood. Dr. Ellis unfortunately died at the early age of 34 years and was succeeded by Dr. Robert Egglesfield

Griffith, who was compelled, by reason of ill-health, to resign his professorship and give up his work on the JOURNAL in 1838. Both Ellis and Griffith have not only left their imprint on the pages of the JOURNAL, but in their Formularies have contributed much to the progress of pharmacy.

The third editor of the JOURNAL was Dr. Joseph Carson, whose editorship ran from 1838–1848. Dr. Carson was one of the ablest men ever connected with our College, his books and his orginal papers being of a very high order. Dr. Carson was succeeded by Professor William Procter, Jr., who held the position for twenty-two years. During his time the numbers issued per year were extended from four to six. Professor Procter was one of the most voluminous contributors, and his name will be revered for many generations to come. Professor Procter was succeeded by Professor John M. Maisch, who held the office from 1871 to 1893, a period of twenty-two years, equal to that of Procter. Professor Maisch was likewise a large contributor and during his time the numbers issued annually were increased to twelve. In 1894, Professor Trimble was elected editor, which position he occupied until 1898, when he died. His untimely death was a great blow to our College, as his enthusiasm and unselfishness were of intrinsic value in adding to the prestige of the JOURNAL. During this time he and Professor Bastin made most valuable contributions to the JOURNAL, these articles even to-day being specially called for. Since 1898, the writer has assumed the duties of editor, a period of eighteen years. *Tempus fugit!* How time flies! As one is going over the material for each issue, he hardly realizes how the work accumulates as the years roll on. By actual measurement, there is a yard-stick of bound volumes which have been added during these eighteen years. Prompted by this thought, I find that there are four yards of volumes contributed during these ninety years. Nearly five generations of workers have labored incessantly to keep burning the lamp of knowledge enkindled by the first Publishing Committee. At no time, probably, has there been more enthusiasm and greater stimulus for the development of the JOURNAL than to-day. As the Atlantic Monthly is the pride of American men of letters, so the AMERICAN JOURNAL OF PHARMACY is the pride of American pharmacists. Our policy has not been to force the ideals of the leaders upon the profession but rather that the pages be like the lamps in our cathedrals, calling attention to the ideals for which we should strive. There has been one purpose, one character, which dominates the pages from the beginning. This has always been of a very high quality and has rung true to the highest ethics. There is no professional journal with such a record, and few scientific journals have such a history.

The past year has been one of great satisfaction to the editor in that there has been a sustained interest among our subscribers and advertisers, and there have been many words of encouragement received. Without desiring to detract from the work of other members, I desire to express my appreciation to our fellow-members, Mr. John K. Thum and Sister Bertha Muller, for their abstracts from foreign sources and their assistance in the columns of Current Literature. I cannot let this opportunity pass without saying a word of grateful recognition of Professor Samuel P. Sadtler, who has been a member of the Publication Committee since 1895, and its chairman during most of these years. His counsel and his sympathy have done much to keep alive the

enthusiasm and ambition of the present editor. His name is so linked with that of the JOURNAL that we trust that, no matter what other positions he may relinquish in the College work, he will continue as a member of the Publication Committee.

On motion, the report was ordered entered and filed.

COMMITTEE ON PHARMACEUTICAL MEETINGS.—The report was read by Professor Kraemer: "During the past year but a single meeting has been held, but what was lacking in numbers has been more than offset by quality. Professor John Uri Lloyd, of Cincinnati, gave us a lecture on "Natural Alkaloidal Structures," which was illustrated by experiments and lantern slides. Quite a few of the members of the College and nearly all of the students who could possibly attend were present. In some respects it was an historic lecture. Professor Lloyd has been a profound investigator in pharmacy for about forty years. His papers have been almost overlooked, and yet they touch so deep that even now Wolfgang Ostwald is having them translated for publication in the "Zeitschrift für Chemie und Industrie der Kolloide." When, on motion, the report was ordered entered and filed.

REPORT OF THE CURATOR.—Read by Mr. Joseph W. England: "The collections of drugs in the Museum of the College embrace many rare and valuable specimens and form probably one of the most valuable in the country. The specimens are derived from animal, vegetable and chemical sources, and have been arranged according to origin. To Professor Kraemer belongs the credit of suggesting that the collections be entirely rearranged along chiefly educational and historical lines, so that they shall be of some popular interest, and under his direction this has been done. The rearranged collections have been labelled through the generosity of our fellow-member, Mr. George B. Evans, whose son has also taken a very deep interest in the work. Special donations have been made illustrating the processes in the manufacture of sugar, which have been sent in by the Franklin Sugar Refining Company. Another collection of much interest is the chemical products obtained from licorice, which have been donated by the McAndrew Forbes Company. A number of monographic collections have also been installed, which are illustrated with large drawings and photographs belonging to Professor Henry Kraemer, who has loaned them to the College. The portraits have been rearranged and displayed to greater advantage." The report was ordered entered and filed.

The Report of the Librarian, Miss Katherine E. Nagle, was read by Joseph W. England.

"The total number of books accessioned to this date is 8899, and up to this time 3195 books have been catalogued. During the past year the use of the Library by the professors and students has materially increased, and it will increase in greater ratio when the catalogue is in condition to be consulted. The number of volumes in the Library is about 14,000, besides several thousand pamphlets. Use of the Library for the year as follows: professors, 189 times; students, 2700 times; public, 101 times.

The report was ordered entered and filed.

Election of Officers and Trustees and Committees.—After the Report of the Committee on Nominations was read, Messrs. Boring and Bernstein were appointed tellers.

Before the ballot was taken, Mr. Warren H. Poley tendered his resignation as a member of the Board of Trustees, he having been nominated for treasurer in place of Richard M. Shoemaker, who declined a renomination. The resignation was accepted and a ballot taken; while the tellers were counting the vote the president made the following appointments:

Committee on By-laws: George M. Beringer, Joseph W. England, C. A. Weidemann.

Delegates to the Pennsylvania Pharmaceutical Association: C. B. Lowe, F. X. Moerk, F. P. Stroup, Charles H. LaWall, E. F. Cook, O. W. Osterlund.

Delegates to the New Jersey Pharmaceutical Association: Joseph P. Remington, George M. Beringer, Charles H. LaWall, H. P. Thorn, John W. Hayes.

Delegates to the Delaware Pharmaceutical Association: A. W. Miller, C. B. Lowe, H. J. Watson, S. Loraine Foster.

The Committee on By-laws proposed an amendment to Section I, Article viii, as follows: "Section I. Any person approving the objects of the College and its code of ethics may be elected an active member." Action was deferred till the next meeting.

The tellers reported the result of the election as follows: President, Howard B. French; 1st Vice-President, R. V. Mattison, M.D.; 2d Vice-President, Joseph L. Lemberger; Treasurer, Warren H. Poley; Corresponding Secretary, A. W. Miller, M.D.; Recording Secretary, C. A. Weidemann, M.D.; Curator, Joseph W. England; Editor, Henry Kraemer; and Librarian, Katharine E. Nagle.

Trustees: Samuel P. Sadtler, William L. Cliffe, H. K. Mulford and R. M. Shoemaker.

Publication Committee: Samuel P. Sadtler, Henry Kraemer, Joseph W. England, Joseph P. Remington, Charles H. LaWall, George M. Beringer and John K. Thum.

Committee on Pharmaceutical Meetings: Henry Kraemer, Joseph P. Remington, C. B. Lowe, M.D., George B. Weidemann and E. H. Hessler.

Mr. Poley, treasurer-elect, asked for the reading of the By-law relating to the duties of the treasurer. This being done, Mr. Poley asked about bonding the treasurer, as the By-laws require. He could give his personal bond if that was satisfactory, or have the College provide a bond from some bonding company. When Mr. Beringer moved that the matter be referred to the Finance Committee of the Board of Trustees with power to act, so ordered.

Professor Kraemer requested to be relieved as chairman of the Committee on Membership and Professor LaWall was elected to the vacated chairmanship.

C. A. Weidemann, M.D.,
Recording Secretary.

ABSTRACTS FROM THE MINUTES OF THE BOARD OF TRUSTEES.

January 4, 1916.—Fourteen members present. Sub-Committee on Instruction reported that 150 students had availed themselves of the opportunity of joining the Y. M. C. A. Two applications for Associate Membership were received. Committee on Instruction submitted the resignation of one of the assistants in botany, which, on motion, was accepted. Professor Kraemer recommended Joseph O'Reilly as student assistant for the second semester, and, on motion, the recommendation was approved.

February 1, 1916.—Thirteen members were present. Committee on Instruction reported in a preliminary way the proposed course in Physiological Assaying and the teaching of German. The Board approved of the general plan, and the committee was instructed to report more fully at a future meeting.

Mr. Beringer read a communication from Professor Sadtler, in which he tendered his resignation as Professor of Chemistry, to take effect June, 1916. Mr. Poley moved that the resignation be accepted

with an expression of deep regret. The Dean spoke very feelingly as to the first break in many years to be made in the Faculty. Mr. Beringer stated that in accepting Professor Sadtler's resignation it was the thought of the committee to ask that he be elected Emeritus Professor of Chemistry, and, therefore, he desired to amend the motion and have the resignation referred to the committee. The amendment was accepted and so ordered.

Professor Sadtler stated that in severing his connection with the College as Professor of Chemistry he intended to keep alive his activities with the College, and would gladly assist in special lecture course or other service.

Mr. Beringer read a communication from Professor Kraemer stating the need of another student assistant for the work of the second semester, and recommended Mr. Harry Ottinger. On motion, the recommendation was approved.

Committee on Examination reported that Louis J. Kleinfeld had finished the course of instruction in Analytical Chemistry, and successfully passed the examinations and is entitled to receive the Certificate of Proficiency in Chemistry. On motion, the certificate was awarded.

The Registrar read a communication from Benjamin C. Quick, Class of 1895, applying for a duplicate diploma, the original having been destroyed by fire. All the requirements having been complied with, it was voted to grant the request.

The Committee on Membership reported favorably on the application of Lloyd P. Griesemer and Philip Fackenthall for Associate Membership. A ballot was taken and they were unanimously elected

---

ABSTRACT OF ADDRESS OF THE PRESIDENT.

In submitting to you a brief summary of matters that have occurred during the past year in your institution, I am following a precedent which was started the first year after I was honored with the presidency of your college.

During the year it has been necessary to make some unusual repairs to your buildings, and if your financial conditions will admit, it will be desirable during the coming summer months to make some improvements which will necessarily require an outlay of considerable money. Although your property is not in bad condition, it is exceedingly desirable to keep it up to a high standard, and it is for this reason that the foregoing suggestion has been made.

The past session of your college was the first to have re-established a two years' course for a Graduate in Pharmacy (Ph.G.) degree. This course was started to meet the educational demands of an adjacent state, the preliminary requirements for entrance being at least one year of completed high school work, or its equivalent of 15 counts. This course will fully equip the student to pass the examinations of State Boards of Pharmacy and will enable him to successfully practise his profession.

Your Board of Trustees have deemed it prudent to retain the three years' course for a Doctor in Pharmacy (Phar.D.) degree, as it had been very popular with those seeking a higher pharmaceutical education than that extended by some of the other pharmacy schools. This course necessarily requires a higher preliminary education; or, in other words, four years of completed high school work, or its equivalent of 60 counts, 45 of which must be credited to the student before entering the first year, and the remaining 15 counts must be obtained by the student before the beginning of the second year. A three years' course leading to the degree of Doctor in Pharmacy (P.D.) was established under the new arrangement and started with the college year in September, 1915. This will not affect, however, those students who have already completed one or two college years under the former plan for a Doctor of Pharmacy (Phar.D.) degree.

In addition to the two courses above referred to, your Board of Trustees have established a course in Chemistry and Pharmacy, leading to a degree of Bachelor of Science in Chemistry and Pharmacy (B.Sc.). This will require a course of four years, the first two being those given in the Graduate in Pharmacy course, and the preliminary educational requirements will be those required for the Doctor of Pharmacy degree.

In addition to this, special courses in Chemistry, Bacteriology, etc., have been established.

The total number of students attending your college this year is 479, being an increase of 48 over the preceding year. The first year matriculants numbered 173, 11 of whom did not begin the course, as their entrance credentials were not sufficiently high to meet the requirements of the college; 17 are in but partial attendance—this makes the number of the first year class 145 members. The second year matriculants number 125, one of whom is not attending, thus making the class 124 in attendance. The third year matriculants number 124, which, together with 19 hold-overs and 5 not attending, leaves the total number of the third year's class at 138.

The Special Chemistry students number 38.

Food and Drug Course has 4 students.

Special Course in Bacteriology has 29 students, one not attending, making 28 in the class, of which 12 students are regular pharmacy students, 4 are graduates of the Philadelphia College of Pharmacy, and 4 taking the Food and Drug course, 4 Special Chemistry students and 4 new matriculants. There are also two students taking special courses.

There are 52 students doing special work in the chemistry laboratory, of which 19 are third year students and 12 of whom are doing thesis work.

It may not be amiss to call your attention to the fact that among those seeking admission to the college for the term 1914–1915, 7 applicants furnished unsatisfactory entrance credentials; while for the term 1915–1916, 6 applicants failed to furnish satisfactory entrance credentials, and 22 who passed the examination did not matriculate.

Your president regrets to note a falling off in the number of students taking special courses in the chemical laboratory, but this, he feels, was brought about by the unusual conditions existing at the opening of the course, owing to the great war now raging between the prominent countries of Europe, and the consequent unusual demand in this country for men possessing more than ordinary business or scientific knowledge—the demand for which has been unprecedented during the last eight or twelve months.

The recording of attendance of students has been continued as during former sessions and it is gratifying to report that it continues to show an improvement over preceding years.

The change authorized by your board establishing a two years' course has necessarily caused considerable labor in the arrangement of lectures, laboratory work and recitations, and it was necessary to exercise the greatest care in order to see that nothing essential was overlooked or left out of the two years' course. This necessitated the taking of a most comprehensive view of all interests, as well as a most intimate consideration of the necessary details, all of which was most heartily entered into by the faculty of your college. The amount of teaching brought about by the change was most unusual, and the instruction given in the department of pharmacy and others was necessarily greatly increased. Extra lectures on pharmaceutical subjects have been largely augmented and the speakers at these

lectures have expressed themselves as being much pleased with the interest which the students took in their addresses.

It is with pleasure that your president reports that this department of your institution has given your students more instruction than was recorded in the roster, and he commends those interested in this department for their activity and enthusiasm.

The new Balopticon lantern installed in the pharmacy lecture room to illustrate upon screens prescriptions, laboratory interiors, special apparatus, etc., has added much to the interest of students in this department.

In operative pharmacy, the course has been most successfully carried on during the session. Originally, operative pharmacy was taught only to the graduating class, but this has now been increased so that all classes in the college receive instruction in this branch, and examinations for promotion are obligatory. In this department, your Committee on Property has erected a large still for distilling water for various departments of your institution, which has proven both economical and most satisfactory.

In the Dispensing Department the students have been taught actual compounding of prescriptions through the selection of typical examples and unusual compounding. They have been instructed in the proper cleaning of bottles, selection of corks, capping of bottles and labelling. Great stress has been placed upon the character of labels used. This instruction, together with what might be termed commercial pharmacy, has aided greatly in preparing young men, not only for their professional careers, but for commercial life. Your college has the honor of being the first institution teaching pharmacy to establish such a training.

The Department of Botany and Pharmacognosy continues to have a steady growth, and it is a pleasure to report that the property entrusted to them has had good, if not unusual, care. The acquisition of 50 new microscopes has aided this department materially and has proven of great benefit to the students. A number of the old microscopes have been sold, yielding a revenue to the college of $472.50, and your professor of this department states that he hopes to dispose of the balance of the old microscopes before the present term is over.

During the past year your professor in this department has gotten out practically a new work on pharmacognosy, which not only does credit to himself but to your institution.

Some interesting research work is being conducted in this laboratory, some of which is of a high character and now has all indications of proving to be of sufficient value to publish in your JOURNAL. One of the subjects being investigated is "The Production of Citric Acid Fermentation by Fungi"; another is "The Morphology and Constituents of the West Indian Cashew-nut," and still another is "The Structure of the Seeds and Pods of Cacao."

Your greenhouse on the roof of your Cherry Street building continues to be of great advantage in the caring for and the studying of medicinal plants. The department expresses the hope that in the near future more extensive facilities for growing plants and studying them at close range may be provided.

It is to be hoped that your institution, at no distant future, may be able to provide for the work in this department which is now almost necessary, and will become more or less imperative with the advanced work which must be expected for the department within the next few years. It is suggested that in this line some thought be given to establishing a memorial in the name of Joseph Carson, whose illustrated work was probably the first to bear the imprint of a professor associated with the Philadelphia College of Pharmacy.

The Martindale Herbarium continues to be of great interest to specialists, and it is to be hoped that arrangements can soon be made to have it cleaned and arranged according to the present system of classification.

Your executive has been in communication with members of the Park Commission trying to arrange to have set aside a space of ground in Fairmount Park to be used as a botanical garden; and while some encouragement has been extended to the project, no definite action has as yet been taken. As stated a year ago, it seems essential that the city or state should assist the educational institutions of Philadelphia in having at their disposal a botanical garden so as to aid in the advanced study of botany and pharmacognosy. It may not be out of place in this connection to suggest that nothing will bring greater lustre to the city of Philadelphia, as a medical centre, than the establishment of such a garden.

Your Department of Bacteriology is meeting with satisfactory results, and the students in same have increased over 30 per cent. It is an interesting fact to note that some of the students in this branch are showing unusual adaptability in this study and it may not require a very great stretch of imagination to state that we can look forward to some of these young men becoming prominent in this line of study and doing credit to their Alma Mater.

During the past year material work has been done in arranging the exhibits in the museum so as to make them more attractive to the visitor. Your surplus specimens have been placed in the old gymnasium, where shelving has been erected to accommodate them; in this way, large quantities of unofficial drugs and specimens are being cared for—many of them in original containers.

Recently, exhibits of licorice and its constituents, as well as exhibits of sugar from its crude to its manufactured form, have been placed in the museum, and your institution is much indebted to the Franklin Sugar Refining Company and the MacAndrews & Forbes Company, Camden, N. J., for these donations.

The portraits in your museum have been rearranged and are now in such a position as to make them far more attractive than in the past.

During the yast year one member has been elected to your organization and one member has died; this leaves your membership as it was a year ago, numbering 141. During the past year two associate members have been elected, making the number now 14. During the year, as stated above, your college lost one member by death, Joseph A. Heintzelman, who died October 19, 1915. He joined the college in 1859 and was a member for 56 years. For many years he was actively interested in the welfare of your institution, and your president wishes to record his regrets at the loss.

Referring to the membership, it seems to your president that a change should be made in your By-laws so as to admit to membership people who are interested in educational pursuits and not to confine your membership, as at present, to those eligible under Section 1, Article VIII, of the By-laws, which reads, "Any graduate in pharmacy, druggist, manufacturing chemist, manufacturing pharmacist, apothecary, or persons associated in allied industries or interests, conforming in professional conduct to the Code of Ethics adopted by this College, may be elected an active member"; and may he not ask whether it would not be better to amend Article VIII to read, "Any person approving the objects of the College and its Code of Ethics may be elected an Active Member"?

It is with extreme regret that your president has to report the resignation of Dr. Samuel P. Sadtler as Professor of Chemistry. He has been connected with your institution for 38 years and has done much to advance the teaching of pharmaceutical chemistry. He has not only honored your institution, but been a great credit to

it, as well as increasing the reputation of Philadelphia as a chemical centre. He leaves your institution on account of pressure of personal work, and it is with extreme regret that your Board of Trustees accepted his resignation, which becomes effective June next. Your Board, however, immediately elected him as Professor Emeritus of Chemistry, in which position he will continue to render assistance to your College and will greatly aid the high standard which it has maintained for so many years in the teaching of chemistry.

Your executive greatly regrets that the health of Richard M. Shoemaker, your treasurer, has forced him to decline re-election. He has, however, kindly consented to serve as a member of your Board, if elected to that position. He has served your organization, as treasurer, for nine years, since the death of his predecessor, James T. Shinn, and is the ninth treasurer that your College has had since its organization in 1821. His father was actively identified with the welfare of the institution and it is the hope of your president that if Mr. Shoemaker is elected to fill an unexpired term on the Board that his life may be spared and that we may have the advantage of his coöperation for many years to come.

Your centenary is rapidly approaching and your institution must look forward to meeting it with outstretched hands, ready to take another advance step in your educational standards. Your president desires to express the hope that the men then in charge will have the courage of their convictions so developed as to enable them to stand up before all odds and contend for what they believe to be right, and he sincerely hopes that the satisfaction of having fought for the right, whether they win or lose, will be sufficient justification for showing to the pharmaceutical world their intention of maintaining the present high standard of your institution as a world's leader of pharmaceutical education.

In closing, your executive wishes to express his appreciation for the hearty coöperation which has been extended to him by those officially associated with the College.

Respectfully submitted,

HOWARD B. FRENCH.

March 27, 1916.